

10/667,167

=> file caplus

FILE 'CAPLUS' ENTERED AT 10:38:51 ON 10 NOV 2004

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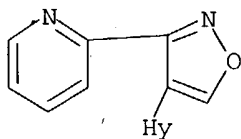
FILE COVERS 1907 - 10 Nov 2004 VOL 141 ISS 20

FILE LAST UPDATED: 9 Nov 2004 (20041109/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que

L1 STR



Structure attributes must be viewed using STN Express query preparation.

L3 7 SEA FILE=REGISTRY SSS FUL L1

L4 2 SEA FILE=CAPLUS L3

=> d l4 1-2 ibib abs hitstr

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:267328 CAPLUS

DOCUMENT NUMBER: 140:287372

TITLE: Preparation of 2-(isoxazol-4-yl)pyridines and related compounds as transforming growth factor (TGF) inhibitors for the treatment of cancer and fibrotic diseases.

INVENTOR(S): Blumberg, Laura Cook; Munchhof, Michael John

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026865	A1	20040401	WO 2003-IB4005	20030912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

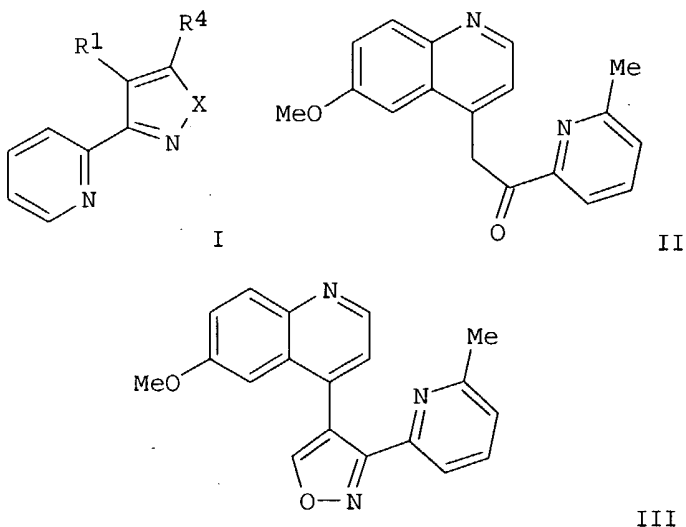
10/667,167

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,  
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,  
MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
GW, ML, MR, NE, SN, TD, TG

US 2004116473 A1 20040617 US 2003-667167 20030917  
PRIORITY APPLN. INFO.: US 2002-412131P P 20020918  
US 2003-484580P P 20030702

OTHER SOURCE(S): MARPAT 140:287372  
GI



AB Title compds. I [X = O, S; R1 = (un)saturated aromatic, monocyclic, bicyclic, etc.; R2 = (R3)s; R3 = H, halo, halo-alkyl, etc.; s = 1-5; R4 = H, halo, alkenyl, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation of ketone II, e.g., prepared from 6-methoxy-4-quinolinecarboxaldehyde in one step, N,N-dimethylformamide di-Me acetal and hydroxylamine afforded isoxazole III. In  $\beta$ 1-transforming growth factors kinase assay, isoxazole III exhibited an IC<sub>50</sub> value of 118 nM. Of note, compds. I also possess differential activity, i.e. are selective for  $\beta$ 1-TGF over  $\beta$ 2-TGF and  $\beta$ 3-TGF. Compds. I are claimed useful for the treatment of TGF-related disease states including cancer and fibrotic diseases.

IT **676256-19-2P**, 4-[3-(6-Methylpyridin-2-yl)isoxazol-4-yl]quinoline  
**676256-20-5P** **676256-21-6P**, 6-[3-(6-Methylpyridin-2-yl)isoxazol-4-yl]quinoxaline **676256-22-7P**, 4-Chloro-6-[3-(6-methylpyridin-2-yl)isoxazol-4-yl]quinoline **676256-23-8P**, 6-Methoxy-4-[3-(6-methylpyridin-2-yl)isoxazol-4-yl]quinoline

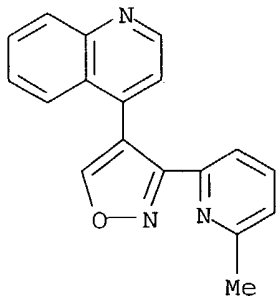
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(isoxazolyl)pyridines and related compds. as transforming growth factor (TGF) inhibitors for the treatment of cancer and fibrotic diseases.)

10/667,167

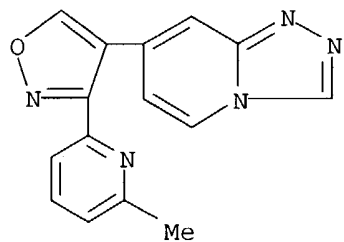
RN 676256-19-2 CAPLUS

CN Quinoline, 4-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



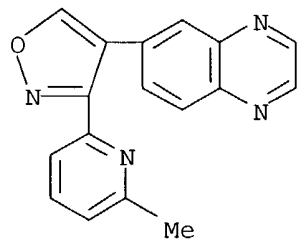
RN 676256-20-5 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyridine, 7-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



RN 676256-21-6 CAPLUS

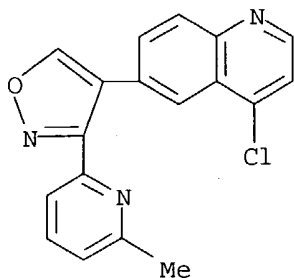
CN Quinoxaline, 6-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



RN 676256-22-7 CAPLUS

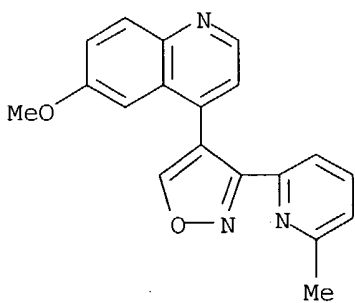
CN Quinoline, 4-chloro-6-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)

10/667,167



RN 676256-23-8 CAPLUS

CN Quinoline, 6-methoxy-4-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:42269 CAPLUS

DOCUMENT NUMBER: 138:106708

TITLE: Preparation of isoxazolylpyrimidines as inhibitors of Src and Lck protein kinases

INVENTOR(S): Bemis, Guy; Gao, Huai; Harrington, Edmund; Ledebor, Mark; Salituro, Francesco; Wang, Jian

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 117 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004492	A1	20030116	WO 2002-US18956	20020614
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

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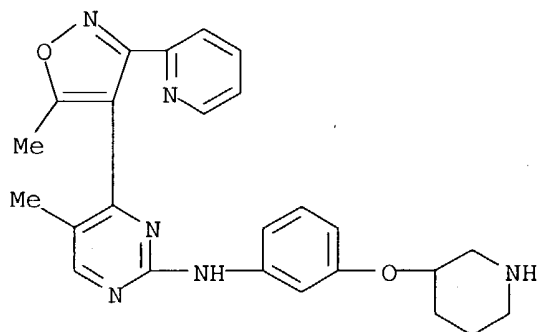
US 2003171389 A1 20030911 US 2002-171895 20020614  
US 6689778 B2 20040210  
EP 1417205 A1 20040512 EP 2002-744355 20020614  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
PRIORITY APPLN. INFO.: US 2001-302969P P 20010703  
WO 2002-US18956 W 20020614  
OTHER SOURCE(S): MARPAT 138:106708  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Isoxazolyipyrimidines [e.g., I; wherein A-B = N-O or O-N; G = alkyl, cycloalkyl, alkoxy, thioalkoxy, aryloxy, alkylsulfoxy, amino, etc.; R1 = H, halo, NO<sub>2</sub>, (substituted) (C1-C6)alkylidene, etc.; R2 = H, (substituted) (C1-C6)alkyl, etc.; R3 = H, alkoxy, thioalkoxy, aryloxy, alkylsulfoxy, amino, etc.; R4 = H, halo, NO<sub>2</sub>, CN, alkoxy, thioalkoxy, amino, amido, etc.] were prepared. For example, 4-(2-{3-[4-(3-cyclohexyl-5-methylisoxazol-4-yl)pyrimidin-2-ylamino]phenoxy}ethyl)piperidin-4-ol (II) was prepared in several steps. These compds. are inhibitors of Src and Lck kinase. For example, compound II provided Ki < 0.1 µM in a Src inhibition assay.

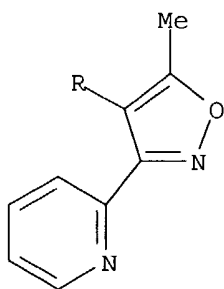
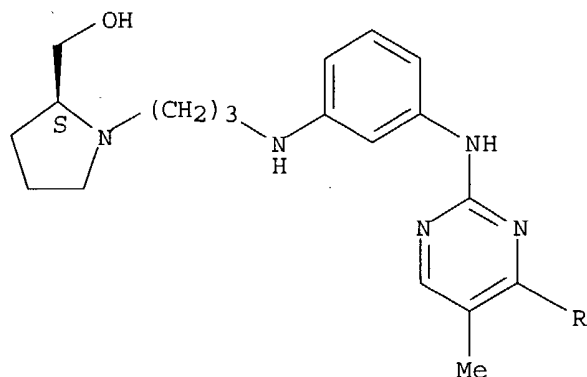
IT **486428-06-2P 486428-47-1P**  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of isoxazolyipyrimidines as inhibitors of Src and Lck protein kinases)

RN 486428-06-2 CAPLUS  
CN 2-Pyrimidinamine, 5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazolyl]-N-[3-(3-piperidinylloxy)phenyl]- (9CI) (CA INDEX NAME)



RN 486428-47-1 CAPLUS  
CN 2-Pyrrolidinemethanol, 1-[3-[[3-[[5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazolyl]-2-pyrimidinyl]aminophenyl]amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

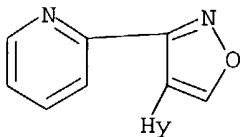


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => file uspatall  
FILE 'USPATFULL' ENTERED AT 10:39:35 ON 10 NOV 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:39:35 ON 10 NOV 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d que  
L1 STR



Structure attributes must be viewed using STN Express query preparation.

L3 7 SEA FILE=REGISTRY SSS FUL L1  
L5 3 SEA L3

=> d 15 1-3 ibib abs hitstr

10/667,167

L5 ANSWER 1 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2004:152251 USPATFULL  
TITLE: Novel isothiazole and isoxazole compounds as  
transforming growth factor (TGF) inhibitors  
INVENTOR(S): Munchhof, Michael J., Salem, CT, UNITED STATES  
Blumberg, Laura C., Waterford, CT, UNITED STATES  
PATENT ASSIGNEE(S): Pfizer Inc (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004116473	A1	20040617
APPLICATION INFO.:	US 2003-667167	A1	20030917 (10)

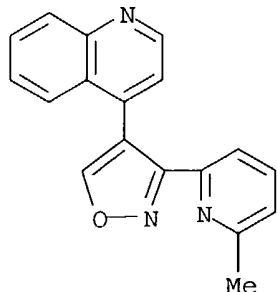
	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-412131P	20020918 (60)
	US 2003-484580P	20030702 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1216	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel isothiazole and isoxazole compounds, including derivatives thereof, to intermediates for their preparation, to pharmaceutical compositions containing them and to their medicinal use are described. The compounds of the present invention are potent inhibitors of transforming growth factor ("TGF")- $\beta$  signaling pathway. They are useful in the treatment of various TGF-related disease states including, for example, cancer, and fibrotic diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

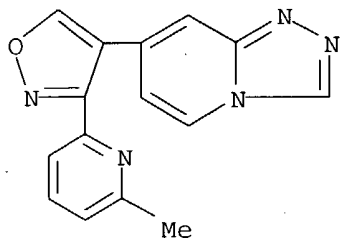
IT **676256-19-2P**, 4-[3-(6-Methylpyridin-2-yl)isoxazol-4-yl]-quinoline  
**676256-20-5P 676256-21-6P**, 6-[3-(6-Methylpyridin-2-yl)isoxazol-4-yl]quinoxaline **676256-22-7P**, 4-Chloro-6-[3-(6-methylpyridin-2-yl)isoxazol-4-yl]quinoline **676256-23-8P**, 6-Methoxy-4-[3-(6-methylpyridin-2-yl)isoxazol-4-yl]quinoline (preparation of 2-(isoxazolyl)pyridines and related compds. as transforming growth factor (TGF) inhibitors for the treatment of cancer and fibrotic diseases.)  
RN 676256-19-2 USPATFULL  
CN Quinoline, 4-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



RN 676256-20-5 USPATFULL

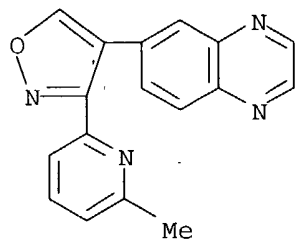
10/667,167

CN 1,2,4-Triazolo[4,3-a]pyridine, 7-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]-  
(9CI) (CA INDEX NAME)



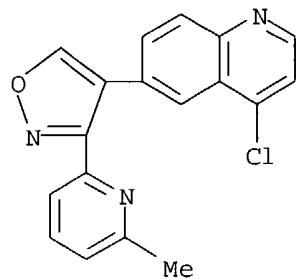
RN 676256-21-6 USPATFULL

CN Quinoxaline, 6-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



RN 676256-22-7 USPATFULL

CN Quinoline, 4-chloro-6-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)

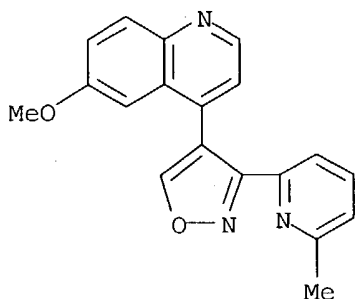


RN 676256-23-8 USPATFULL

CN Quinoline, 6-methoxy-4-[3-(6-methyl-2-pyridinyl)-4-isoxazolyl]- (9CI) (CA INDEX NAME)



10/667,167



L5 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2003:244975 USPATFULL  
TITLE: Inhibitors of Src and Lck protein kinases  
INVENTOR(S): Bemis, Guy, Arlington, MA, UNITED STATES  
Gao, Huai, Natick, MA, UNITED STATES  
Harrington, Edmund, South Boston, MA, UNITED STATES  
Salituro, Francesco, Marlboro, MA, UNITED STATES  
Wang, Jian, Boston, MA, UNITED STATES  
Ledebor, Mark, Acton, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003171389	A1	20030911
	US 6689778	B2	20040210
APPLICATION INFO.:	US 2002-171895	A1	20020614 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-302969P	20010703 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA, 02139-4242	
NUMBER OF CLAIMS:	34	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1734	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides compounds of formula I: ##STR1##

or a pharmaceutically acceptable derivative thereof, wherein A-B is N--O or O--N and G, R.sup.1, R.sup.2, R.sup.3, and R.sup.4 are as described in the specification. These compounds are inhibitors of protein kinase, particularly inhibitors of Src and Lck kinase. The invention also provides pharmaceutical compositions comprising the inhibitors of the invention and methods of utilizing those compositions in the treatment and prevention of various disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

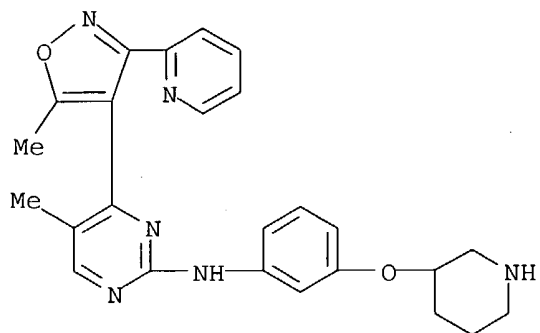
IT 486428-06-2P 486428-47-1P

(preparation of isoxazolyipyrimidines as inhibitors of Src and Lck protein kinases)

RN 486428-06-2 USPATFULL

CN 2-Pyrimidinamine, 5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazoly]l-N-[3-(3-piperidinyloxy)phenyl]- (9CI) (CA INDEX NAME)

10/667,167

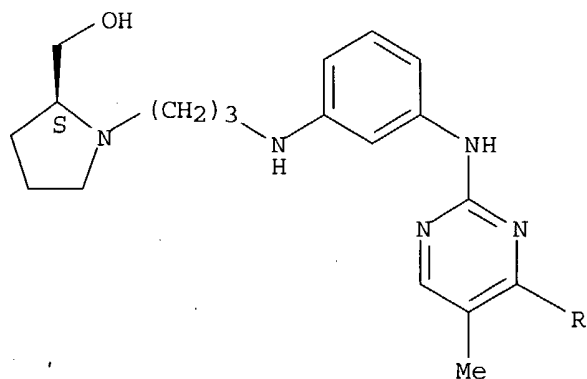


RN 486428-47-1 USPATFULL

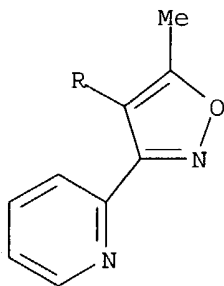
CN 2-Pyrrolidinemethanol, 1-[[3-[[3-[[5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazolyl]-2-pyrimidinyl]amino]phenyl]aminopropyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L5 ANSWER 3 OF 3 USPAT2 on STN

ACCESSION NUMBER: 2003:244975 USPAT2

TITLE: Inhibitors of Src and Lck protein kinases

INVENTOR(S): Bemis, Guy, Arlington, MA, United States  
Gao, Huai, Natick, MA, United States

10/667,167

Harrington, Edmund, South Boston, MA, United States  
Salituro, Francesco, Marlboro, MA, United States  
Wang, Jian, Boston, MA, United States  
Ledeboer, Mark, Acton, MA, United States  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, Cambridge, MA,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6689778	B2	20040210
APPLICATION INFO.:	US 2002-171895		20020614 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-302969P	20010703 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Rao, Deepak	
LEGAL REPRESENTATIVE:	Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	1647	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides compounds of formula I: ##STR1##

or a pharmaceutically acceptable derivative thereof, wherein A--B is N--O or O--N and G, R.sup.1, R.sup.2, R.sup.3, and R.sup.4 are as described in the specification. These compounds are inhibitors of protein kinase, particularly inhibitors of Src and Lck kinase. The invention also provides pharmaceutical compositions comprising the inhibitors of the invention and methods of utilizing those compositions in the treatment and prevention of various disorders.

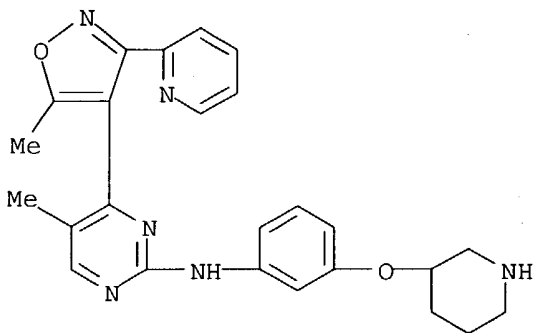
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 486428-06-2P 486428-47-1P

(preparation of isoxazolympyrimidines as inhibitors of Src and Lck protein kinases)

RN 486428-06-2 USPAT2

CN 2-Pyrimidinamine, 5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazoly]-N-[3-(3-piperidinyloxy)phenyl]- (9CI) (CA INDEX NAME)



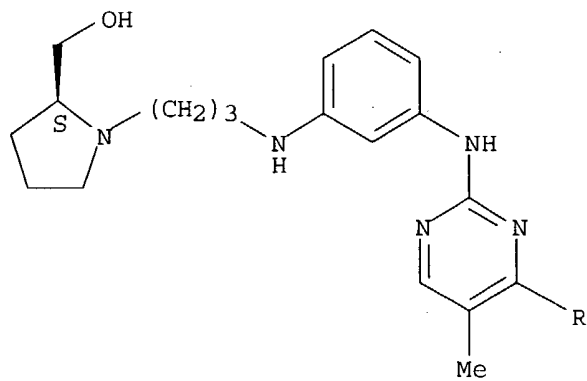
RN 486428-47-1 USPAT2

CN 2-Pyrrolidinemethanol, 1-[3-[[3-[[5-methyl-4-[5-methyl-3-(2-pyridinyl)-4-isoxazoly]-2-pyrimidinyl]amino]phenyl]amino]propyl]-, (2S)- (9CI) (CA INDEX NAME)

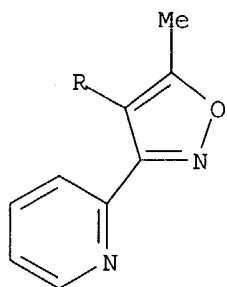
10/667,167

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



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